REMARKS

Claims 73-84 were pending. Claims 73-84 were cancelled. Claims 85-90 were added. Therefore, claims 85-90 will be pending upon entry of the present amendment.

No new matter has been added. Support for the new claims can be found through out the specification as originally filed. In particular, support for new claim 85 can be found, for example, at least in claim 1 as originally filed and in the specification at page 8, line 19 and page 25, lines 10-17. Support for new claim 86 can be found, for example, at least in claim 1 as originally filed and in the specification at page 4, line 36, page 8, line 18, and page 25, line 10-17. Support for new claim 87 can be found, for example, at least in claim 1 as originally filed and in the specification at page 6, lines 11-15 and page 25, line 10-17. Support for new claim 88 can be found, for example, at least in claim 5 as originally filed and in the specification at page 25, line 25. Support for new claim 89 can be found, for example, at least in claim 19 as originally filed and in the specification at page 25, line 23-24. Support for new claim 90 can be found, for example, at least in claim 91 as originally filed and in the specification at page 4, line 24 through page 5, line 2.

Applicants would like to thank the Examiner and Examiner Fredman for the telephonic interview that took place on June 29, 2005 between them and Applicants' attorneys.

Applicants would like to reiterate the arguments made in their Amendment and Response of May 27, 2005.

Rejection of the Claims under 35 U.S.C. § 102(b)

Claims 56-58 and 60-62 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,871,712 ("Siman"). Claims 56-58 and 60-62 were cancelled in the amendment of May 27, 2005, thus rendering their rejection moot. To the extent that the Siman reference may be applied against the presently claimed invention, Applicants present the following arguments for patentability.

The present invention is directed to identifying small molecules relevant to amyotrophic lateral sclerosis. Although, Siman describes a method for detecting pathological conditions related to calpain-generated spectrin BDP's, Siman does not teach nor suggest that the methods described therein would be applicable to pathological conditions not related to calpain-generated spectrin BDP's, like amyotrophic lateral sclerosis.

The Siman reference describes a method for detecting calpain activation by detecting levels of calpain-generated spectrin BDP's using antibodies that specifically bind to these proteins. By design, Siman's antibodies only detect spectrin BDPs, and do not detect small molecule profiles. Accordingly, the reference fails to anticipate the claims. The reference only teaches detection of spectrin BDPs, not more than one type of small molecule, let alone 50% or more of the small molecules in the sample as required by Applicants. Siman also fails to teach or suggest detecting both electrochemically active and electrochemically neutral small molecules as required by claim 86. Furthermore, Siman's antibodies only detect spectrin BDP's which are polypeptides, and not sugars, fatty acids, amino acids, nucleotides, metabolites, and products of catabolism, as claimed in claim 87.

Therefore, Applicants respectfully submit that Siman does not teach or suggest the presently claimed invention and request that the rejection by reconsidered and withdrawn.

Rejection of the Claims under 35 U.S.C. § 102(e)

Claims 56-62 were rejected under 35 U.S.C. § 102(e) as being anticipated by Niebroj-Dobosz *et al.* (*Acta Neurol. Scan.* 1999 100:6-11). Applicants submit that claims 56-62 have been cancelled in the amendment of May 27, 2005, thus rendering their rejection moot. To the extent that the Niebroj-Doboscz *et al.* reference may be applied against the presently claimed invention, Applicants present the following arguments for patentability.

Niebroj-Dobosz *et al.* is directed to confirming the hypothesis that amino acids act as transmitters in amyotrophic lateral sclerosis. Niebroj-Dobosz used HPLC to test for the presence of excitotoxic amino acids.

In Niebroj-Dobosz *et al.*, the presence of four amino acids were studied: aspartate, glutamate, glycine, and GABA. The techniques used by Niebroj-Dobosz are specific to removing the amino acids of interest from the sample through pre-column derivitization with florescent agents and then passing the derivatized amino acids through an HPLC column. The techniques used by Niebroj-Dobosz *et al.* only detect the amino acids of interest to them, and not 50% or more of the small molecules in the sample as claimed by Applicants in claim 85.

In Niebroj-Dobosz *et al.*, the HPLC methods described therein are selected to separate electrochemically active molecules which react with the florescent detectors. The fluorescent detectors used by Niebroj-Dobosz *et al.* are by design specifically for the amino acids of interest to them. The methods of Niebroj-Dobosz *et al.* are specific to the

particular amino acids studied and not to a diverse group of electrochemically active and electrochemically neutral small molecules as claimed by Applicants in claim 86.

Niebroj-Dobosz *et al.* is directed to proving the hypothesis that ALS results in an imbalance of excitatory and inhibitory amino acids. Niebroj-Dobosz *et al.* does not teach or suggest a method for identifying small molecules relevant to ALS by comparing a small molecule profile comprising information regarding two or more types of small molecules selected from the group consisting of: sugars, fatty acids, amino acids, nucleotides, metabolites, and products of catabolism in claim 87. In contrast, the methods described by Niebroj-Dobosz are specific to the amino acids which were previously identified.

Therefore, Applicants respectfully submit that Niebroj-Dobosz *et al.* does not teach or suggest the presently claimed invention.

SUMMARY

Cancellation of and/or amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The cancellation of and/or amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The amendments made to the claims are not related to any issues of patentability.

In view of the above remarks and amendments, it is believed that this application is in condition for allowance. If a telephone conversation with Applicant's Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call Elizabeth A. Hanley, Esq. at (617) 227-7400.

Date: August 5, 2005

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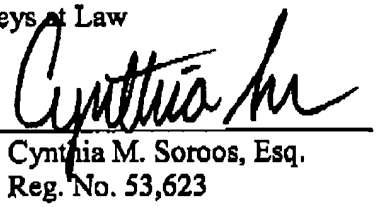
Attorneys at Law

By 

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